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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,427	01/18/2001	Linda Hockersmith	IMET0050	7093

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EXAMINER
GITOMER, RALPH J

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 07/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/766,427	Applicant(s) Hockersmith
	Examiner Ralph Gitomer	Art Unit 1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 28, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3, 5, 8-12, 24, 26, 28, 31-33, and 35* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3, 5, 8-12, 24, 26, 28, 31-33, and 35* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 10
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The amendment, IDS, and Declaration received 5/28/2003 have been received and claims 1, 3, 5, 8-12, 24, 26, 28, 31-33, 35 are currently pending in this application.

Claims 1, 3, 5, 8-12, 24, 26, 28, 31-33, 35 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

In claim 35 the preamble is directed to a method of generating a glycemic profile but the claim lacks the steps required to do so. The last phrase of claim 35, ▒wherein a resulting glycemic profile to factors other than subject's blood glucose concentration▒ is not understood in context where no other factors appear to be considered. Glycemic profiles are generally correlated to blood glucose concentration and not to other factors. No controls are claimed. Further, what the glycemic profile results from is not seen. Claim 35 is not understood because the rate of change of glucose concentration must correspond to a target rate. In claim 1 ▒said required amount of carbohydrate▒ lacks antecedent basis and does not state what it is required for. In claim 1 ▒target maximum▒ is not defined as to what it may be or how it is obtained. In claim 1 no units are described which would make such a calculation

difficult depending upon the units selected. How would one know how much carbohydrate is determined if there are no units? Further, to perform the calculation one would need to know the starting blood glucose concentration, the target glucose concentration and X, and how these are obtained, assigned, estimated, or calculated is not set forth. As claimed, X could be anything. The method of claim 14 requires ingesting an ▒estimated required amount▒ of carbohydrate which is calculated according to the formula in the claim which is based on a value ▒X▒. The value ▒X▒ is somehow obtained/generated after the step of ingesting the ▒required amount▒ of carbohydrate. Thus two unknown variables, CHO and X, are present in the single equation and it is not clear how one of CHO and X is initially determined such that the other of CHO and X can be determined using the formula. If any of the variables are arbitrary, then the result would necessarily be arbitrary. Further, the equation of claim 1 uses the symbol CHO for a different value than claim 8. Claim 9 is directed to a second actual amount of carbohydrate but how it is calculated and its function is not set forth. Claim 11 is not understood in context as to how one achieves a profile based on some unstated formula. Claim 12 is not understood as to how the model would be calibrated and ▒anti-correlated▒ is not understood in context. Claim 32 is not understood because there are no steps to accomplish the method.

Applicant's arguments filed 5/28/2003 have been fully considered but they are not persuasive.

Applicant argues that the specification teaches the invention of claim 35. The declaration describes various units of glucose concentration and it is known how to determine glucose concentration. The invention is not directed to establishment or selection of target values but how to achieve a target value. Calculating X is based upon the clinician's knowledge of objective criteria. Calibration of blood glucose values requires uncorrelated factors. The invention is not directed to target values but how to achieve a target value. X is not a calculated value but an assigned value.

The requirement of 35 U.S.C. § 112 second paragraph that the claims particularly point out and distinctly claim the invention are not met by the claims in their present form. Therefore, the metes and bounds intended for the claims cannot be ascertained.

It is the examiner's position that the above rejection is based upon the claims as presented, not the teachings of the specification or Declaration. As written, one would not know how to calculate the required variables to practice the invention. No target values are claimed and as stated, one cannot calculate any target values. X as a constant dependent on units of other variables would be standard in such calculations. No objective criteria of assigning any value to X is seen in the claims. The

claims are not directed to calibration but to a glycemic profile and how such unknown factors can be anti-correlated is not seen. No assignment of any specific value to X is claimed.

Claims 1, 3, 5, 8-12, 24, 26, 28, 31-33, 35 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling.

The selection of a target maximum and a target minimum are critical to determine the rate of change of glucose concentration. Further, how X is calculated is critical or essential to the practice of the invention, but not included in the claim(s), nor is it set forth in the specification. Therefore, the feature is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Applicant's arguments filed 5/28/2003 have been fully considered but they are not persuasive.

Applicant argues that the target rate of change is established by the target glycemic profile which is shown in the specification. The target is not critical to the invention and may be arbitrary. Since X is an arbitrary value, it does not need to be calculated. The Declaration states that one of skill in this art would know how to calculate X.

It is the examiner's position that the claimed invention is based upon solving an equation to determine a variable and if each of the expressions in the equation are arbitrary variables, then the solution is arbitrary and not solvable. One of skill in this art would not know how to calculate X as claimed.

Claims 1, 3, 5, 8-12, 24, 26, 28, 31-33, 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

On page 4 under Summary of the Invention, a point of novelty may be ▒a novel numerical index that quantifies the subject's sensitivity to carbohydrate.▒ This index appears to be critical to developing an optimal glycemic profile. In the claims this index is represented as X. How X is calculated is not described in such a fashion to enable one of skill in this art to perform the calculation. On page 13 last paragraph bridging to page 14, a description of X and Xi is provided in general terms insufficient to be reproduced. On page 14 Table 4 has no units. A reading of page 15 would appear to imply the point of novelty is optimizing insulin relative to meal times but how to perform such optimization is not taught. It is well known in this art that the type of insulin and dose of insulin will alter the rate

of change of glucose level. And the type of food eaten and the quantity of food eaten will affect the rate of change of glucose level.

On page 5 last paragraph, reference blood glucose values are obtained that are uncorrelated to sampling factors such as skin temperature, environmental temperatures, time of day and other blood analytes. How this is performed is not set forth.

On page 6 first paragraph, the invention provides a method of calibrating a noninvasive blood glucose monitor using blood glucose reference values in which correlating to sampling factors previously mentioned is greatly reduced or eliminated. This method is not set forth.

Critical to the invention is the target values such as those set forth in page 8 last paragraph. How these values were selected and their particular significance is not set forth.

On page 9, noninvasive and invasive measurements of blood glucose were made. The significance of performing both is not seen.

On page 9 Table 1 the A1C of the subjects is all relatively low indicating good glucose control. It is understood that a A1C of under 7 generally indicates adequate blood glucose control. How the present invention would relate to those subjects with good glucose control is not seen.

On page 10 Table 2 indicates results of some treatment but what the treatment was has not been set forth. Also, significantly, there was a desired selected maximum and minimum but how the treatment was designed to achieve those values has not been set forth. If the max and min are not at the selected levels, then what? How is this test customized to obtain the desired information? It should be expected that some subjects are more sensitive to a given amount of carbohydrate and insulin than others. On page 11 a more aggressive insulin dosing regimen produced different values. What was this regimen and how was it determined?

On page 12 first paragraph, the rate of change desired is 1.33. How was this determined and what is its significance? Would the rate of change of increase be desired to be the same as rate of change of decrease of blood glucose concentration? On page 12 Table 3 shows results of some unknown treatment for rate of change which varies greatly. What is the significance of this? That some subjects require more carbohydrate or insulin? On page 14 first paragraph, assigning a numerical value to carbohydrate sensitivity is discussed in the absence of glycemic index, glycemic load and many other dietary factors. No mention is made of the type of carbohydrate consumed, only an amount based on generalized factor X.

Applicant's arguments filed 5/28/2003 have been fully considered but they are not persuasive.

Applicant argues that the invention is directed to an optimal glycemic profile. A formula is not a mathematical expression. The description is enabling to one having ordinary skill in the art. X has no units and CHO intake is expressed in grams. Methods of controlling blood glucose levels are disclosed in the specification. It is known how to calibrate noninvasive blood glucose monitors. Target values are arbitrary. The specification describes a treatment. The selected rate of change is arbitrary. The type of carbohydrate consumed would be known by one skilled in the art and are carefully selected foods. It is known in the art how to dose insulin. The selected (arbitrary) target values are based on an index indicative of the subject's carbohydrate sensitivity.

It is the examiner's position that the specification does not teach one of skill in this art how to calculate an optimal glycemic profile. The claims require a calculation to determine something which cannot be performed as claimed. The basis of this rejection under 35 USC 112, first paragraph, is upon one of skill in this art. To be useful, one would need to calculate an amount of carbohydrate which requires units. To perform such a calculation in a useful manner has certain requirements. The treatment based upon the calculation is not disclosed in the

specification beyond eating carbohydrates that are carefully selected in some unknown manner.

It has been interpreted that the intended invention may be a method of elevating glucose from a starting value to a selected target value by administering an amount of carbohydrate determined by some formula. It is well known in this art that diabetics regularly determine their serum glucose concentration to adjust the dose of insulin and the amount they eat in order to keep their glucose concentration within some selected range. It remains unclear as to how the present invention differs from this well known procedure. The Declaration provided by the Applicant does little more than further this argument.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5, 8-12, 24, 26, 28, 31-33, 35 are rejected under 35 U.S.C. 102(b) as being anticipated by each of Galen, Volpicelli and Liszka-Hackzell.

Galen (5,695,949) entitled ▒Combined Assay for Current Glucose Level and Intermediate or Long Term Glycemic Control▒ teaches in column 1, lines 30-35, some patients measure their blood glucose levels up to seven times a day. Based on the observed pattern in the measured glucose levels, the patient and physician together make adjustments in diet, exercise and insulin intake to better manage the disease. In column 4 lines 19-31 various desired levels of glucose concentration are shown.

Volpicelli (Clinical Physiology) entitled ▒Controlled Oral Glucose tolerance Test: Evaluation of Insulin Resistance With an Insulin Infusion Algorithm That Forces The OGTT Glycaemic Curve Within The Normal Range▒ teaches in the summary, insulin is infused to keep glucose within the normal range to assess a glycemic curve. On page 33 column 1, a glucose load and insulin are administered according to an algorithm to force the glycemic curve to remain within the normal range of values. On page 40 column 1 last paragraph, parameters are standardized for carbohydrate intake, and time.

Liszka-Hackzel (Computers and Biomedical Research) entitled ▒Prediction of Blood Glucose Levels in Diabetic Patients Using a Hybrid Technique▒ teaches in the summary, balancing the dose of insulin and glucose concentration with an algorithm. On page 132 last paragraph, glucose level is adjusted by insulin dose and diet. Throughout the article, timing is discussed for eating and insulin dosing. See page 142 Fig. 9 shows predicted glucose levels vs. Observed glucose levels.

Claims 1, 3, 5, 8-12, 24, 26, 28, 31-33, 35 rejected under 35 U.S.C. 102(a) as being anticipated by Brown.

Brown (5,956,501) entitled ▒Disease Simulation System and Method▒ teaches math models, in column 2 first full paragraph, simulating the effect of changes in insulin and diet on the blood glucose profile of a patient. In column 5 a mathematical model to calculate disease control parameter values is described based on time intervals. For a daily rhythm control parameter such as a blood glucose level, the time points are preferably before and after meals. A diabetic patient parameter values include a prescribed dose of insulin, a prescribed intake of carbohydrates, and a prescribed exercise duration. In column 6 last paragraph, parameters include insulin sensitivity. In column 7, the amount of insulin based on sensitivity is used to calculate how much a unit of insulin is expected to lower glucose level. In column 9, amounts of carbohydrates consumed is calculated to obtain an

optimal value. See the claims.

All the features of the claims are taught by each of the above references for the same function.

Regarding claim 3 directed to conventional foods, the above references teach diabetic people eating conventional foods. Regarding claim 12 directed to a calibration method for use in non-invasive methods of blood glucose determination employing spectroscopic instrumentation, the method of Brown is deemed to be inherently usable with known non-invasive methods of glucose determinations.

Applicant's arguments filed 5/28/2003 have been fully considered but they are not persuasive.

Applicant argues that Galen does not concern generating a glycemic profile have a predetermined shape with a target rate of change. Volpicelli maintains the glycemic curve about a steady state where the present invention requires a target maximum and minimum. And Volpicelli does not have a profile that is uncorrelated to other factors. Liszka-Hackzel does not concern a glycemic profile having a predetermined shape that is uncorrelated. Brown is not concerned with a glycemic profile having a predetermined shape that is uncorrelated. And Brown is concerned with insulin sensitivity.

Much of Applicant's arguments are centered upon unclaimed limitations, such as a shape of a glycemic curve, specific target values, uncorrelated factors. It is respectfully submitted that in order for evidence of unexpected results to be sufficient to rebut a prima facie case of obviousness, the evidence must be commensurate in scope with the claims.

Galen teaches how to make adjustments in diet to manage diabetes which appears to be the object of the presently claimed invention. This is the same as generating a glycemic profile of a predetermined shape with a target rate of change. Volpicelli teaches an algorithm related to glucose load and insulin administered with a number of parameters described. This would require some (arbitrary) target maximum and minimum values. Liszka-Hackzel teaches balancing the dose of insulin and glucose with an algorithm. Brown teaches glycemic profiles of predetermined shapes correlated to a number of factors including exercise, food intake, timing, insulin dose, and insulin sensitivity. To predict an appropriate amount of carbohydrate to ingest or generate a glycemic profile, based upon no units and arbitrary values, not correlated to some unknown factors, is clearly taught by each of the above references which are all directed to determining how much carbohydrate and insulin are best employed to maintain blood glucose levels between some target minima and maxima values.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (703) 308-0732. The examiner can normally be reached on Tuesday-Friday from 8:00 am - 5:00 pm. The examiner can also be reached on alternate Mondays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (703) 308-4743. The fax phone numbers for this Art Unit are before

final (703) 872-9306 and after final (703) 872-9307. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235. For 24 hour access to patent application information 7 days per week, or for filing applications electronically, please visit our website at www.uspto.gov and click on the button ▒Patent Electronic Business Center▒ for more information.

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